

CLAIMS

- Ins. a1*
1. The use of an extract from *Aristolochia taliscana* or one or more anti-mutagenically active compounds isolable therefrom for the manufacture of a medicament for the treatment of disease states mediated by mutagenesis.
 2. The use of an extract from an *Aristolochia* species such as *Aristolochia taliscana* or one or more component compounds isolable therefrom for the manufacture of a medicament for the treatment of chronic inflammatory diseases such as inflammatory bowel disease, rheumatoid arthritis, synovitis and psoriasis.
 3. The use of an extract from *Aristolochia taliscana* or one or more antifungally active compounds isolable therefrom for the manufacture of a composition for antifungal use, for example in the treatment of fungal infections in animals, or for use in the treatment of fungal infections in plants.
 4. The use according to any one of claims 1 to 3 wherein the composition contains at least 10%, preferably at least 20%, and more preferably at least 25% by weight of a phenylbenzofuran.
 5. The use according to claim 4 wherein the phenylbenzofuran is a eupomatenoid.
 6. The use according to claim 4 or claim 5 wherein the phenylbenzofuran contains a phenolic group.
 7. The use according to claim 6 wherein the phenylbenzofuran is eupomatenoid-7.
 8. The use according to any one of the preceding claims wherein the composition contains Licarin-A.
 9. The use according to any one of the preceding claims wherein the

composition contains a cytotoxic tetralone compound.

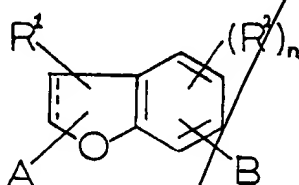
10. The use according to any one of the preceding claims wherein the composition contains a 2-hydroxy-1-tetralone compound.
11. The use according to claim 9 or claim 10 wherein the tetralone compound is (2R,4S)-2-Hydroxy-6-methoxy-4,7-dimethyl-1-tetralone.
12. The use according to any one of the preceding claims wherein the composition contains at least 25% by weight of a phenolic eupomatenoid compound (such as eupomatenoid-7), at least 8% of Licarin-A and at least 8% of a non-phenolic eupomatenoid compound (such as eupomatenoid-8).
13. The use according to any one of the preceding claims wherein the composition contains an aristolactam.
14. The use according to any one of the preceding claims wherein the extract has been prepared by extraction of plant material from the *Aristolochia* species with an organic solvent.
15. The use according to claim 14 wherein the organic solvent is an alcoholic solvent such as ethanol or methanol or a mixture thereof.
16. The use according to claim 14 wherein the organic solvent is benzene, the solvent having been removed from the extract prior to use.
17. A method of treating a disease state mediated by mutagenesis, which method comprises administering to a patient suffering from said disease state an effective antimutagenic treatment amount of an extract from an *Aristolochia* species or one or more antimutagenic compounds isolable therefrom, as defined in any one of the preceding claims.
18. A method of inhibiting mutagenesis in an organism, which method comprises administering to the organism an effective antimutagenic amount

of an extract from *Aristolochia taliscana* or one or more antimutagenic compounds isolable therefrom, as defined in any one of the preceding claims.

19. A method of producing a cytotoxic effect in an organism (such as an animal), which method comprises administering to the organism in an amount effective to produce the cytotoxic effect an extract from *Aristolochia taliscana* or one or more cytotoxic compounds isolable therefrom, as defined in any one of the preceding claims.
20. A method of preventing or treating a fungal infection in an animal patient such as a human, which method comprises administering to the patient an effective antifungal amount of an extract from *Aristolochia taliscana* or one or more antifungal compounds isolable therefrom, as defined in any one of the preceding claims.
21. A method of preventing or treating a fungal infection in a plant, which method comprises administering to the plant an effective antifungal amount of an extract from *Aristolochia taliscana* or one or more antifungal compounds isolable therefrom, as defined in any one of the preceding claims.
22. A method of inhibiting fungal growth in a substrate, which method comprises administering to the substrate an antifungal effective amount of an extract from *Aristolochia taliscana* or one or more antifungal compounds isolable therefrom, as defined in any one of the preceding claims.
23. A method according to claim 22 wherein the substrate is selected from animal (e.g. mammals such as humans) and plant tissues.
24. A method of treating a chronic inflammatory disease such as inflammatory bowel disease, rheumatoid arthritis, synovitis or psoriasis in a patient, which method comprises administering to the patient an effective amount of an extract from an *Aristolochia* species such as *Aristolochia taliscana* or one or

more component compounds isolable therefrom.

25. The use of a compound for the manufacture of a medicament for use in any one or more of the therapeutic uses selected from the treatment of neoplastic diseases or diseases mediated or initiated by mutagenesis or abnormal cellular proliferation, or as a cytotoxic agent, or the treatment of chronic inflammatory conditions, the compound being of the formula (I):



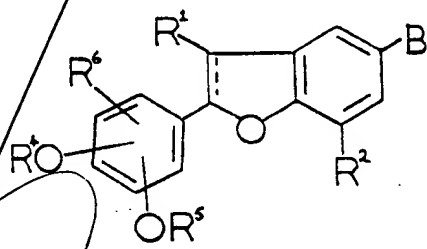
(I)

wherein the dotted line signifies a single or double bond; n is 0, 1, 2 or 3; A is a monocyclic aryl ring optionally substituted by one or more substituent groups which may be the same or different and are selected from R^3O , R^3 , R^3S , halogen; aryl and heteroaryl, wherein R^3 is hydrogen, or a hydrocarbyl group optionally substituted by a hydroxy or hydrocarbyloxy group; B is selected from carboxy, carboxaldehyde, hydrocarbyl and hydrocarbyloxy groups wherein the hydrocarbyl group is acyclic or cyclic, and optionally contains one or more heteroatoms, and is optionally substituted by one or more hydroxy, alkoxy, alkenyloxy, alkynyloxy, aryloxy, aldehyde, alkanoyl, acetal, hemiacetal and carboxy groups; R^1 is hydrogen or a hydrocarbyl group optionally including one or more heteroatoms and optionally substituted by one or more substituents selected from hydroxy, hydrocarbyloxy and aryl groups; and R^2 is hydroxy or a hydrocarbyl or hydrocarbyloxy group optionally substituted by one or more substituents selected from hydroxy, hydrocarbyloxy and aryl groups.

26. The use according to claim 25 wherein the monocyclic aryl ring A is attached to the 2-position of the furan ring.

41

27. The use according to claim 25 or claim 26 wherein the aryl ring is a phenyl group.
28. The use according to any one of claims 25 to 27 wherein the group B is attached to the 5-position of the benzofuran group.
29. The use according to any one of claims 25 to 28 wherein there is only one group R^2 .
30. The use according to claim 29 wherein the group R^2 is attached to the 7-position of the benzofuran ring.
31. The use according to any one of claims 25 to 30 wherein the dotted line signifies a double bond.
32. The use according to claim 25 wherein the compound of the formula (I) has the formula (II):



(II)

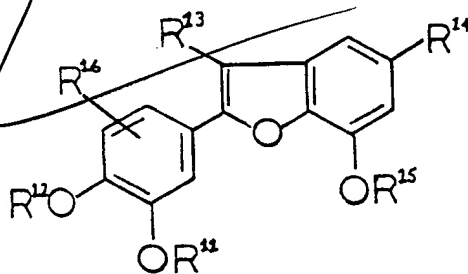
wherein B, R^1 and R^2 are as defined in any one of claims 25 to 31, R^4 and R^5 are the same or different and each is selected from hydrogen, C_{1-20} hydrocarbyl, C_{5-20} aryl, or C_{5-20} oxygen-containing heteroaryl; R^6 is selected from hydrogen, halogen, C_{1-20} hydrocarbyl or C_{1-20} hydrocarbyloxy optionally substituted by one or more hydroxy, alkoxy, aralkyloxy groups; or R^6 is C_{5-25} aryl or oxygen or nitrogen-containing heteroaryl.

33. The use according to claim 32 wherein B is C_{1-6} alkyl or alkenyl optionally substituted by one or more substituents selected from hydroxy, CHO, or R^7O wherein R^7 is a C_{1-6} alkyl or alkenyl group.

42

34. The use according to claim 33 wherein the group B is selected from $\text{CH}=\text{CHCH}_3$, $\text{CH}_2\text{CH}=\text{CH}_2$, $\text{CH}(\text{OH})\text{CH}=\text{CH}_2$, $\text{CH}=\text{CHCHO}$, CHO , $\text{CH}=\text{CHCH}_2\text{OH}$ and $\text{CH}(\text{OH})\text{CH}(\text{OH})\text{CH}_3$.
35. The use according to claim 34 wherein B is $\text{CH}=\text{CHCH}_3$.
36. The use according to any one of claims 25 to 35 wherein R^4 and R^5 are selected from hydrogen, or C_{1-6} alkyl, or R^4 and R^5 together define an alkylene group such as $-\text{CH}_2-$.
37. The use according to claim 36 wherein at least one of R^4 and R^5 is hydrogen.
38. The use according to any one of claims 32 to 37 wherein R^6 is selected from hydrogen, halogen, C_{1-6} alkoxy (e.g. methoxy), a 2-benzofuranyl ring, and an aristolactam group.
39. The use according to any one of claims 25 to 38 wherein each hydrocarbyl group is selected from aliphatic, alicyclic and aromatic groups.
40. The use according to claim 39 wherein the hydrocarbyl group is selected from alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, cycloalkylalkenyl, cycloalkylalkynyl, aryl, aralkyl, aralkenyl, aralkynyl, optionally interrupted by one or more heteroatoms such as oxygen and sulphur.
41. The use according to claim 40 wherein the hydrocarbyl group is a C_{1-6} alkyl group selected from methyl, ethyl, propyl, isopropyl, butyl, isobutyl and t-butyl; a cycloalkyl group selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, bicycloheptanyl, decalanyl, adamantyl, norbornyl and bicyclooctyl; an alkenyl or alkynyl groups selected from vinyl, ethynyl, allyl, 1-propenyl, propargyl, but-1-enyl, but-2-enyl, but-3-enyl and 3-methylbutenyl; a cycloalkenyl group selected from cyclopentenyl, cyclohexenyl and cycloheptenyl; an aryl groups selected from phenyl and naphthyl; or a phenylalkyl or phenylalkenyl groups selected from benzyl, phenethyl, phenylpropyl, phenylbutyl and styryl groups.

42. A compound of the formula (I) or (II) as defined in any one of the preceding claims for use in medicine, for example for use in any one or more of the therapeutic uses selected from the treatment of neoplastic diseases or diseases mediated or initiated by mutagenesis or abnormal cellular proliferation, or as a cytotoxic agent, or the treatment of chronic inflammatory conditions, or as an anti-fungal agent in the treatment of fungal infections in plants or animals; but provided that when R¹ is 3-methyl, R² is a single methoxy group at the 7-position, and either (i) the furan ring is unsaturated and is substituted at the 2-position with a 4-hydroxy-3-methoxyphenyl group or a 3,4-methylenedioxyphenyl group; or (ii) the furan ring is a 2,3-dihydrofuran ring and is substituted at the 2-position with a 4-hydroxy-3-methoxyphenyl group, then B is other than a prop-1-enyl group attached to the 5-position of the benzofuran ring.
43. A pharmaceutical composition comprising a compound of the formula (I) or (II) as defined in claim 42 together with a pharmaceutically acceptable carrier.
44. A compound of the formula (III):



wherein R¹¹ is hydrogen or C₁₋₆ alkyl;

R¹² is selected from hydrogen, C₁₋₆ alkyl; a cyclic terpenoid group or a group of the formula E, G or J;

R¹³ is selected from hydrogen; C₁₋₃ alkyl or hydroxy-C₁₋₃ alkyl;

R¹⁴ is selected from CH=CH-CH₃, CH(OH)CH=CH₂, CH=CH-CHO,

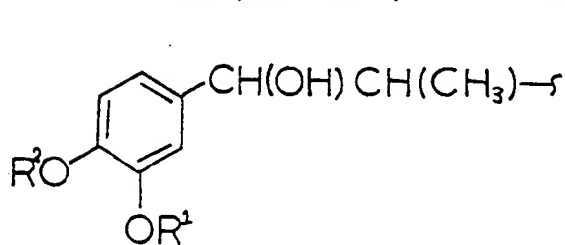
$\text{CH}=\text{CH}-\text{CH}_2\text{OH}$, $\text{CH}(\text{OH})\text{CH}(\text{OR}^{17})\text{CH}_3$, or a group L;

R^{15} is hydrogen or C_{1-6} alkyl;

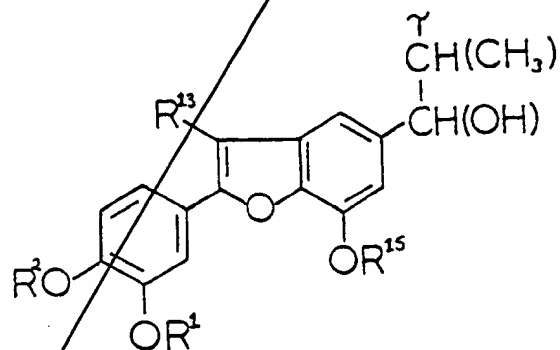
R^{16} is hydrogen, a group M or an aristolactam group; and

R^{17} is hydrogen or a group T; wherein the groups E, G, L, J, M and

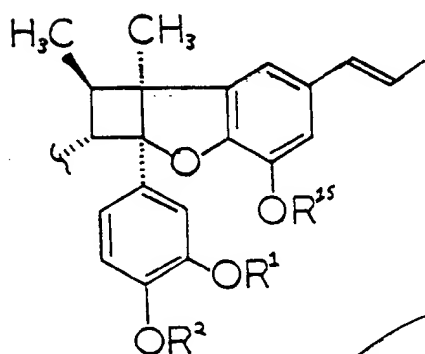
T are represented by the formulae:



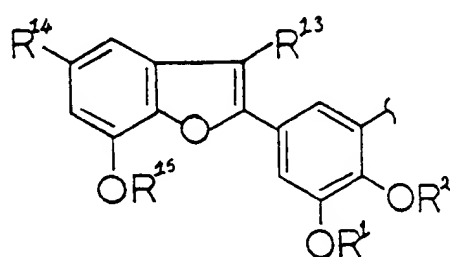
(E)



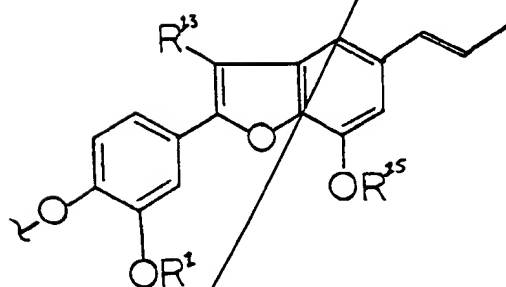
(G)



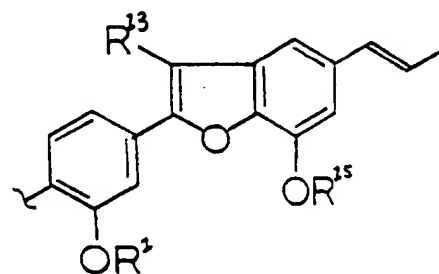
(L)



(J)



(M)

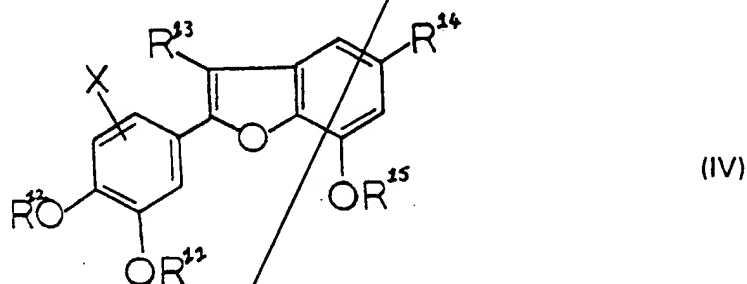


(T)

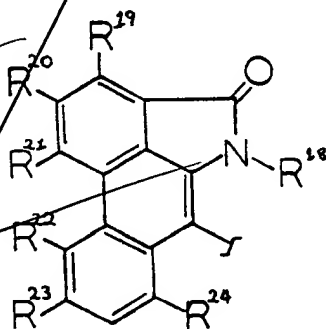
45

and pharmaceutically acceptable salts thereof, provided that when R^{11} , R^{13} and R^{15} are all methyl, and R^{12} and R^{16} are both hydrogen, R^{14} is selected only from $\text{CH}(\text{OH})\text{CH}=\text{CH}_2$, $\text{CH}=\text{CH}-\text{CHO}$, $\text{CH}=\text{CH}-\text{CH}_2\text{OH}$, $\text{CH}(\text{OH})\text{CH}(\text{OR}^{17})\text{CH}_3$ where R^{17} is a group T, or a group L.

45. A compound of the formula (IV):



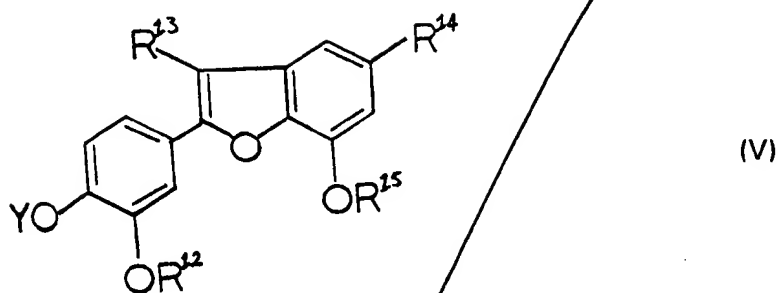
wherein R^{11} , R^{12} , R^{13} , R^{14} , R^{15} and R^{17} are as defined in claim 25 and X is a group:



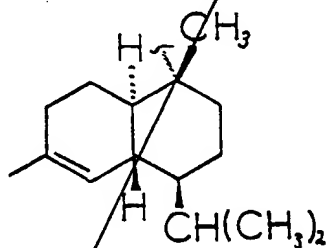
wherein R^{18} is hydrogen, benzyl or C_{1-6} alkyl; R^{19} to R^{24} are the same or different and are selected from hydrogen, hydroxy, C_{1-6} alkoxy, C_{1-6} alkyl and hydroxy- C_{1-6} alkyl; or any two adjacent groups together form an alkylene dioxy group.

46

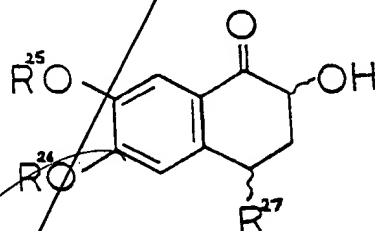
46. A compound of the formula (V):



wherein Y is a monocyclic or bicyclic terpenoid group and in particular a group of the structure:



47. A tetralone compound of the formula (VI):



wherein R^{25} and R^{27} are the same or different and each is C_{1-6} alkyl; and R^{26} is hydrogen or C_{1-6} alkyl, or R^{25} and R^{26} together form an alkylene-dioxy group.

48. A compound according to claim 47 wherein R^{25} , R^{26} and R^{27} are all methyl.
49. A compound according to claim 47 or 48 for use as a biocide.
50. A compound according to claim 49 for use in the treatment of fungal infections, or for use in the treatment of cancers and other proliferative diseases such as psoriasis.

51. A compound selected from the group consisting of:
- (±)-5-(1-Hydroxyallyl)-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-3-methylbenzofuran;
 - 2-(4-Hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-5-(E)-propenylbenzofuran;
 - 2-(4-Hydroxy-3-methoxyphenyl)-7-methoxy-3-methyl-5-[(E)-3-oxopropenyl]benzofuran;
 - 5-Formyl-3-(4-hydroxy-3-methoxyphenyl)-7-methoxy-3-methylbenzofuran;
 - 2-(4-Hydroxy-2-methoxyphenyl)-5-[(E)-3-hydroxypropenyl]-7-methoxy-3-methylbenzofuran;
 - 2-(3,4-Dihydroxyphenyl)-7-methoxy-3-methyl-5-(E)-propenylbenzofuran;
 - erythro*-5-(1,2-Dihydroxypropyl)-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-3-methylbenzofuran;
 - (2R,3R)-2,3-Dihydro-2-(4-hydroxy-3-methoxyphenyl)-3-hydroxymethyl-7-methoxy-5-(E)-propenylbenzofuran;
 - erythro*-1-(4-Acetoxy-3-methoxyphenyl)-2-[4-(7-methoxy-3-methyl-5-(E)-propenylbenzofuran-2-yl)-2-methoxyphenoxy]propylacetate;
 - threo*-1-(4-Acetoxy-3-methoxyphenyl)-2-[4-(7-methoxy-3-methyl-5-(E)-propenylbenzofuran-2-yl)-2-methoxyphenoxy]propyl-acetate;
 - threo*-1-[2-(4-Hydroxy-3-methoxyphenyl)-7-methoxy-3-methylbenzofuran-5-yl]-2-[4-(3-methyl-5-(E)-propenylbenzofuran-2-yl)-2-methoxyphenoxy]propan-1-ol;
 - 2-Methoxy-4-[7-methoxy-3-methyl-5-(E)-propenylbenzofuran-2-yl]-6-[4-(7-methoxy-3-methyl-5-(E)-propenylbenzofuran-2-yl)-2-methoxyphenoxy]phenol;
 - 8,2',9,3'-Tetrahydro-bis-eupomatenoid-7;
 - 15-(Aristolactam-1-9-yl)-eupomatenoid-7;
 - 14-O- α -Cadinyl-eupomatenoid-7; and
 - (2R,4S)-2-Hydroxy-6-methoxy-4,7-dimethyl-1-tetralone.
52. A pharmaceutical composition comprising a compound as defined in any one claims 44 to 51 together with a pharmaceutically acceptable carrier.